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EXAMINER	
NEGIN, RUSSELL SCOTT	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/660,110	OLDHAM ET AL.	
	Examiner	Art Unit	
	RUSSELL S. NEGIN	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20,23-34 and 36-55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20,23-34 and 36-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2 October 2008 has been entered.

Claims 20, 23-34, and 36-55 are pending and examined in the instant Office action.

Applicant's arguments, see page 11 of the Remarks, filed 2 October 2008, with respect to the rejection(s) of claim(s) 20, 23-34, and 36-55 under 35 U.S.C. 103 have been fully considered and are persuasive. Therefore, the rejections have been withdrawn. However, upon further consideration, a new ground(s) of rejection is made under 35 U.S.C. 103 in view of the combination of Savory et al. [Clinical Chemistry, volume 14, 1968, pages 132-144] in view of Hanai [HPLC: A Practical Guide, 1999, pages 23-25] in view of Chen et al. [Genome Research, 1998, volume 8, pages 549-556].

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

<u>The following rejection is newly applied:</u>

<u>35 U.S.C. 102 Rejection #1:</u>

Claims 20, 23-27, 33-34, 36-39, and 45-50 are rejected under 35 U.S.C. 102(e) as being anticipated by Sagatelyan et al. [US Patent 6,894,264 B2; issued 17 May 2005; filed 15 October 2002]. This reference is referred to as Sagatelyan et al. (2005) throughout this Office action.

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Discussion of Independent claims 20, 33, and 45:

Claim 20 is drawn to a method for extending the dynamic range of a photodetector, the method comprising:

--providing a photodetector configured in a first configuration comprising a first dynamic range having a first upper limit;

--performing a first measurement of the identifiable signals with the photodetector at the first configuration such that the photodetector yields a first output signal representing the abundance of a first type of particles, and yields a second output signal representing the abundance of a second type of particles;

--configuring the photodetector to a second configuration comprising a second dynamic range having a second upper limit that is greater than the first upper limit;

--performing a second measurement of the identifiable signals with the photodetector at the second configuration such that the photodetector yields a third output signal representing the abundance of the first type of particles, and yields a fourth output signal representing the abundance of the second type of specific particles, the first output signal exceeds the first upper limit, and the particles of the first type of particles are more abundant in the sample than the particles of the second type of particles;

--determining that the first output signal falls outside of the first dynamic range by determining that the first output signal is greater than the first upper limit; and

--combining the first measurement and the second measurement to determine a scaled representation of the first output signal at the first configuration, wherein the scaled representation of the first output signal represents an output signal that was not within the dynamic range of the photodetector in the first configuration.

Claim 33 is a method drawn to similar subject matter as instant claim 20 without requiring populations of particles to be present in the sample.

Claim 45 is analogous to claim 20 except instead of signals above thresholds of detection being assessed, thresholds below limits of detection are measured.

The invention of Sagatelyan et al. (2005) describes a system and methods for dynamic range extension using variable length integration time sampling.

Specifically, Figure 1 of Sagatelyan et al. (2005) illustrates the photodetector used to study a plurality of different species of nucleic acid particles. Figure 1c, in particular, illustrates a higher abundance (i.e. intensity) of the first peak relative to the second peak. (The first peak in Figure 1C of Sagatelyan et al. (2005) has an intensity above the photodetector dynamic range limit).

The second paragraph of the summary (from column 1, line 65 to column 2 line 21 of Sagatelyan et al. (2005)) describes the method for dynamic range extension involving acquiring two signal components during two respective and different time intervals. Additionally, in this section and in lines 22-34 of column 2 of Sagatelyan et al. (2005), a procedure is outlined for how to scale a first signal component that exceeds the dynamic range (whether above or below the range is not restricted in Sagatelyan et al. (2005)) based on the relative magnitudes a second component that does not exceed the dynamic range of the photodetector. (i.e. If in one configuration the first and second components of the signal are within range, but in the second configuration a single

component is out of range, relative scalings are described to assess the component that is not in range as recited in the instant claims).

With regards to claim 23-24, 34, 36 and 46-47, the scaling procedures in column 2, lines 22-34 of Sagatelyan et al. (2005) along with Figure 1 of Sagatelyan et al. (2005) describe the scaling procedure such that the first and second signals (first and second components in the first configuration wherein the first component is out of range) are based on relative scalings of the third and fourth signals (first and second components in the second configuration wherein both components are in range).

With regard to claims 25-27, 37-39 and 48-50, the plurality of different times (exposure durations) are shown in Figure 5 of Sagatelyan et al. (2005) wherein differences and ratios are computed.

<u>The following rejection is newly applied:</u>

<u>35 U.S.C. 102 Rejection #2:</u>

Claims 20, 23-27, 33-34, 36-39, and 45-50 are rejected under 35 U.S.C. 102(e) as being anticipated by Sagatelyan et al. [US Patent 7,067,791 B2; issued 27 June 2006; benefit date 15 October 2002]. This reference is referred to as Sagatelyan et al. (2006) throughout this Office action.

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art

under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention “by another,” or by an appropriate showing under 37 CFR 1.131.

Independent claims 20, 33, and 45 are discussed above, and are reiterated.

The invention of Sagatelyan et al. (2006) describes a system and methods for dynamic range extension using variable length integration time sampling.

Specifically, Figure 1 of Sagatelyan et al. (2006) illustrates the photodetector used to study a plurality of different species of nucleic acid particles. Figure 1c, in particular, illustrates a higher abundance (i.e. intensity) of the first peak relative to the second peak. (The first peak in Figure 1C of Sagatelyan et al. (2006) has an intensity above the photodetector dynamic range limit).

The third paragraph of the summary (from column 2, lines 7-28 of Sagatelyan et al. (2006)) describes the method for dynamic range extension involving acquiring two signal components during two respective and different time intervals. Additionally, in this section and in lines 29-41 of column 2 of Sagatelyan et al. (2006), a procedure is outlined for how to scale a first signal component that exceeds the dynamic range (whether above or below the range is not restricted in Sagatelyan et al. (2006)) based on the relative magnitudes a second component that does not exceed the dynamic range of the photodetector. (i.e. If in one configuration the first and second components of the signal are within range, but in the second configuration a single component is out

of range, relative scalings are described to assess the component that is not in range as recited in the instant claims).

With regards to claim 23-24, 34, 36 and 46-47, the scaling procedures in column 2, lines 29-41 of Sagatelyan et al. (2006) along with Figure 1 of Sagatelyan et al. (2006) describe the scaling procedure such that the first and second signals (first and second components in the first configuration wherein the first component is out of range) are based on relative scalings of the third and fourth signals (first and second components in the second configuration wherein both components are in range).

With regard to claims 25-27, 37-39 and 48-50, the plurality of different times (exposure durations) are shown in Figure 5 of Sagatelyan et al. (2006) wherein differences and ratios are computed.

<u>The following rejection is newly applied:</u>

<u>35 U.S.C. 102 Rejection #3:</u>

Claims 20, 23-27, 33-34, 36-39, and 45-50 are rejected under 35 U.S.C. 102(e) as being anticipated by Sagatelyan et al. [US Patent 7,423,251 B2; issued 9 September 2008; benefit date 15 October 2002]. This reference is referred to as Sagatelyan et al. (2008) throughout this Office action.

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art

under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Independent claims 20, 33, and 45 are discussed above, and are reiterated.

The invention of Sagatelyan et al. (2008) describes a system and methods for dynamic range extension using variable length integration time sampling.

Specifically, Figure 1 of Sagatelyan et al. (2008) illustrates the photodetector used to study a plurality of different species of nucleic acid particles. Figure 1c, in particular, illustrates a higher abundance (i.e. intensity) of the first peak relative to the second peak. (The first peak in Figure 1C of Sagatelyan et al. (2008) has an intensity above the photodetector dynamic range limit).

The third paragraph of the summary (from column 2, lines 11-32 of Sagatelyan et al. (2008)) describes the method for dynamic range extension involving acquiring two signal components during two respective and different time intervals. Additionally, in this section and in lines 33-45 of column 2 of Sagatelyan et al. (2008), a procedure is outlined for how to scale a first signal component that exceeds the dynamic range (whether above or below the range is not restricted in Sagatelyan et al. (2008)) based on the relative magnitudes a second component that does not exceed the dynamic range of the photodetector. (i.e. If in one configuration the first and second components of the signal are within range, but in the second configuration a single component is out

of range, relative scalings are described to assess the component that is not in range as recited in the instant claims).

With regards to claim 23-24, 34, 36 and 46-47, the scaling procedures in column 2, lines 33-45 of Sagatelyan et al. (2008) along with Figure 1 of Sagatelyan et al. (2008) describe the scaling procedure such that the first and second signals (first and second components in the first configuration wherein the first component is out of range) are based on relative scalings of the third and fourth signals (first and second components in the second configuration wherein both components are in range).

With regard to claims 25-27, 37-39 and 48-50, the plurality of different times (exposure durations) are shown in Figure 5 of Sagatelyan et al. (2008) wherein differences and ratios are computed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

<u>The following rejection is newly applied:</u>

<u>35 U.S.C. 103 Rejection #1</u>:

Claims 20, 23-24, 33-34, 36 and 45-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Savory et al. [Clinical Chemistry, volume 14, 1968, pages 132-144] in view of Hanai [HPLC: A Practical Guide, 1999, pages 23-25] in view of Chen et al. [Genome Research, 1998, volume 8, pages 549-556].

The method of claims 20, 33, and 45 are drawn to improving the assessment of a plurality of types of specific particles in a sample using a photodetector. This photodetector detects particles, each type of particle being labeled with a specific probe. A scaling procedure with two configurations of the photodetector is used such that scaling may be used between configurations to estimate the signals out of the dynamic range of the photodetector in a specific configuration. These independent claims are discussed in more detail in the preceding anticipatory prior art rejections.

Claims 23-24 and 46-47 are further limiting with regards to scaling and combining the signals between the two types of configurations.

Claim 34 is further limiting wherein the first component of the detectable signal is stronger than the second component.

Claim 36 is further limiting wherein scaling the first output signal allows representation of both the first and second components when the dynamic range associated with the detector is limiting and would not be able to measure the first component at the first configuration

The study of Savory et al. investigates an improved procedure for the determination of serum ethanol by gas chromatography. Specifically, Figure 5 on page 141 of Savory et al. illustrates the chromatograms of a single sample of six different compounds obtained in two different configurations of the GC apparatus (Helium flow= 75 ml per min and 45 ml per min, respectively). In this second configuration, the peaks are lower in height than in the first configuration (i.e. while the y axis or dynamic ranges of the chromatograms go to 8 cm and 10 cm, respectively for each of the two configurations, some of the peaks in the first configuration would be out of the dynamic range of the detector in the second configuration).

However, Savory et al. does not show actual scaling between the configurations, nor does he use a photodetector to detect the presence of particles labeled with probes (Savory et al. use a detector)

The text of Hanai studies HPLC spectra.

Specifically, Figure 2.11 on page 24 of Hanai plots peak intensities of a four component aromatic mixture as a function of several variables, one of the variables being flow rate.

When the ratios of the area of peak 1 (benzene) to peak 4 (naphthalene) are plotted as a function of carrier fluid flow rate as they are in lines C and D of Figure 2.12 on page 24 of Hanai, the lines are constant with zero slope (within experimental error). As is stated on the first two lines of page 25, "The peak area ratio between peaks 1 and 4 was almost constant from 1 to 4 ml min^{-1} (Figure 2.12, lines C and D)...."

However, Savory et al. and Hanai do not detect the presence of particles labeled with probes.

The study of Chen et al. is a homogeneous ligase mediated DNA diagnostic test.

Figures 1 and 2 of Chen et al. illustrate an assay and the result of a DOL assay with FRET detection using probes to label the nucleic acid segments. Figure 3 of Chen et al. illustrates the fluorescence intensity profiles of a PCR-DOL assay.

It would have been obvious for someone of ordinary skill in the art at the time of the instant invention to modify the gas chromatography study of Savory et al. by scaling peak size to obtain signals out of range of the detector by using the constant peak area ratio as a function of flow rate principle of Hanai wherein the motivation would have been that since ratios of areas under peaks in chromatograms (i.e. Figure 5 of Savory et al. OR Figure 2.11 of Hanai) are related to the amount of sample injected and are ***independent of flow rate***, taking the ratio of area of peak A to the area of peak B in the second configuration (i.e. where both peaks are within the dynamic range of the detector; i.e. Hanai takes such ratios in Figure 2.12) would have allowed the measurement of the size/abundance of unknown peak A in the first configuration wherein the area of peak B in the first configuration is known. It would have been

further obvious for someone of ordinary skill in the art at the time of the instant invention to modify the detector analysis of Savory et al. by use of the photodetector analysis of Chen et al. because it is obvious to substitute known elements in the prior art to yield a predictable result. In this instance, both types of detector yield the predictable result of sample quantities. There would have been a reasonable expectation of success in combining Savory et al., Hanai, and Chen et al. because in this instance, the detectors and photodetector are used for the same purpose.

Response to Arguments:

Applicant's arguments filed 2 October 2008 have been fully considered, and they are persuasive. The reference of Hanai is used to address the deficiencies of the prior rejection.

Applicant argues since both signals in Figure 5 of Savory et al. are detectable in both configurations, "Savory does not resolve anything at the slower [gas] speed that would not have been readable at the faster speed." This argument is not persuasive (in view of the newly applied reference of Hanai) because peak A in the faster helium flow of Figure 5 has a size in centimeters greater than the threshold value of 8 centimeters for the slower helium flow. When the faster helium flow is imposed in the situation wherein the threshold of 8 centimeters of the slower flow is maintained, peak A would be above the detection limit (i.e. 8 centimeters). As Hanai illustrates that peak area ratio is independent of flow rate, once the peak area is calculated for the peaks within the range of detection, their ratio of areas will not change as a function of flow rate, and

therefore it is obvious to measure the size of a potential peak outside the limits of detection by knowing this ratio and a peak size within the limit of detection. Consequently, this combination of references is not deficient; the reference of Chen et al. is utilized for illustrating the obviousness of using photodetectors for detecting labeled particles.

The following rejection is newly applied:

35 U.S.C. 103 Rejection #2:

Claims 28-29, 40-41, and 51-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Savory et al. in view of in view of Hanai in view of Chen et al. as applied to claims 20, 23, 24, 33, 34, 36, and 45-47 above, and further in view of Tomlinson et al [Electrophoresis, 1994, volume 15, pages 62-71].

Claims 28, 40, and 51 are further limiting wherein the detector is a charge multiplier and the first configuration comprises an operating voltage V1.

Claims 29, 41, and 52 are further limiting wherein the second configuration comprised an operating voltage V2, wherein the operating voltage V2 is higher (or lower for claim 52) than the operating voltage V1.

The studies of Savory et al., Hanai, and Chen et al. make obvious the measurement of signals of particle using photodetectors/detectors, as discussed above.

Savory et al., Hanai, and Chen et al. do not teach use of differing voltages.

Tomlinson et al. discloses two separate voltages for the two separate configurations disclosed in Figures 3 and 4; one configuration uses a voltage of 20kV,

the second uses a voltage of 30 kV- a voltage greater than in the first configuration. (For claim 52, the configurations are interpreted to be reversed).

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the chromatography study of Savory and the photodetector study of Chen et al. by use of the electropherograms analyzed at differing voltages using a photodetector of Tomlinson et al. wherein the motivation would have been that altering voltages in measuring the composition of a sample is an additional means of assessing and comparing relative concentrations of each species of particle in a sample; for example, changing the voltage in Figures 3 and 4 of Tomlinson et al. improves the resolution of the electropherogram.

Response to arguments:

Applicant's arguments filed 2 October 2008 have been fully considered and they are persuasive. Applicant argues that the reference of Tomlinson et al. does not overcome the alleged deficiencies of Savory et al., and Chen et al. For the reasons discussed above, the newly applied combination of Savory et al., Hanai, and Chen et al. is not deficient and the instant prior art rejection is maintained.

The following rejection is newly applied:

35 U.S.C. 103 Rejection #3:

Claims 31-32, 43-44, and 54-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Savory et al. in view of Hanai in view of Chen et al. in view of

Tomlinson et al. as applied to claims 20, 23, 24, 28-29, 33, 34, 36, 40-41, 45-47, and 51-52 above, and further in view of Photomultiplier Tubes [Hamamatsu Brochure, pages 1-15, July 2002].

Claims 31, 43, and 54 are further limiting wherein the charge multiplier comprises photomultiplier tubes.

Claims 32, 44, and 55 are further limiting wherein the charge multiplier comprises a charge intensifier.

The studies of Savory et al., Hanai, Chen et al., and Tomlinson et al. make obvious the measurement of signals of particle using photodetectors, as discussed above.

However, Savory et al., Hanai, Chen et al., and Tomlinson et al. do not disclose charge multipliers, specifically, in the forms of photomultiplier tubes and charge intensifiers.

The catalog "Photomultiplier tubes" discusses uses and sales of photomultiplier tubes and charge intensifiers throughout the brochure.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the photodetector studies of Savory et al., Hanai, Chen et al., and Tomlinson et al. by use of the photomultiplier tubes and charge intensifiers of the Hamamatsu Brochure because it would have been obvious to apply a known technique to a known method to yield a predictable result. In this instance, it would have been obvious to apply the techniques of using photomultipliers and charge intensifiers to the methods of signal analysis of Savory et al., Hanai, Chen et al., and

Tomlinson et al. to result in modified electropherogram absorbance intensities. There would have been a reasonable expectation of success in incorporating the photomultiplier tubes into the detectors of Savory et al., Hanai, Chen et al., and Tomlinson et al. because such photomultiplier tubes and charge multipliers provide an alternative means for measuring the intensities of particles in a mixture (i.e. a photomultiplier detects photons and converts them into electropherograms or electrical signals).

Response to arguments:

Applicant's arguments filed 2 October 2008 have been fully considered and they are persuasive. Applicant argues that the reference of “Photomultiplier tubes” does not overcome the alleged deficiencies of Savory et al., Chen et al., and Tomlinson et al. For the reasons discussed above, the combination of Savory et al., Hanai, Chen et al., and Tomlinson et al. is not deficient and the instant prior art rejection is maintained.

The following rejection is newly applied:

35 U.S.C. 103 Rejection #4:

Claims 30, 42, and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Savory et al. in view of Hanai in view of Chen et al. in view of Tomlinson et al. in view of Photomultiplier tubes (Hammatsu brochure) as applied to claims 20, 23-24, 28-29, 31-34, 36, 40-41, 43-47, 51-52, and 54-55 above, in further view of Priebe [19^{th} Annual Symposium of Frequency Control, 1965, pages 487-508].

Claims 30, 42, and 53 are further limiting wherein the combining to determine comprises determining a scaled value N1 of the first output signal based on the third output signal and the relationship log (N1) = m log (V2/V1) wherein m represents a slope of a curve obtained by plotting the multiplier's gain versus the voltage in a log-log manner.

The studies of Savory et al., Hanai, Chen et al., Tomlinson et al. and the Photomultiplier Tube brochure make obvious the measurement of signals of particle using photomultipler tubes, as discussed above.

Savory et al., Hanai, Chen et al., Tomlinson et al. and the Photomultiplier Tube brochure do not discuss the specific relation in the instant set of claims.

The study of Priebe investigates the attenuation and resistance measurements of unwanted modes of quartz crystals.

Specifically, equation 2 of Priebe shows that the attenuation of the signal from the crystal (in Decibel) is proportional to the logarithm of the ratios of two voltages with the proportionality constant (m) being 20.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the photodetector measurements using photomultiplier tubes of Savory et al., Hanai, Chen et al., Tomlinson et al. and Hamamatsu (i.e. Brochure) by further use of the relation of Priebe because it would have been obvious to apply a known technique to a known method to yield a predictable result. In this instance, it would have been obvious to apply the known signal attenuation techniques of Priebe to the photodetector system of Savory et al., Hanai, Chen et al., Tomlinson et

al. to yield the predictable outcome of comparably attenuated signals. There would have a reasonable expectation of success in combining the relations of Priebe with photomultiplers tubes and detectors of Savory et al., Hanai, Chen et al., Tomlinson et al. because the relation of Priebe allows for the attenuation of a multiplier's gain.

Response to arguments:

Applicant's arguments filed 2 October 2008 have been fully considered and they are persuasive. Applicant argues that the reference of Priebe does not overcome the alleged deficiencies of Savory et al., Chen et al., Tomlinson et al., and "Photomultiplier tubes" For the reasons discussed above, the newly applied combination of Savory et al., Hanai, Chen et al., Tomlinson et al. and "Photomultiplier tubes" is not deficient and the instant prior art rejection is maintained.

The following rejection is newly applied:

35 U.S.C. 103 Rejection #5:

Claims 25-26, 37-38, and 48-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Savory et al. in view of Hanai in view of Chen et al. in view of Tomlinson et al. as applied to claims 20, 23, 24, 28-29, 33, 34, 36, 40-41, 45-47, and 51-52 above, and further in view of Tacklind et al [US PGPUB 2003/0101605; issued 5 June 2003; filed 4 December 2001].

Claims 25, 37, and 48 are further limiting wherein the detector is a charge-coupled device and the first configuration comprises an exposure duration T1.

Claims 26, 38, and 49 are further limiting wherein the second configuration comprises an exposure duration T2, wherein the exposure duration T2 is longer (or shorter for claim 49) than the exposure duration T1.

The studies of Savory et al., Hanai, Chen et al., and Tomlinson et al. make obvious the measurement of signals of particle using photodetectors, as discussed above.

Tomlinson et al. plots two separate migration times for the two separate configurations, with one set (i.e. CE-DAD or Figure 4) having a greater length in migration time (T2) than solely CE (CE is Figure 3, or T1). Depending on which of claims 48-49 are being analyzed, the configuration assignments could be reversed so that T2 is shorter in duration that T1.

However, Savory et al., Hanai, Chen et al., and Tomlinson et al. do not disclose a charge multiplier.

The invention of Tacklind et al. studies servo-controlled automatic level and plumb tool and explains the use of charge coupled devices in paragraph [0060] where it is stated that "The position sensitive photo sensor can incorporate any of a number of commercially available position sensitive detectors sensitive to the detector light… Examples include charged coupled detectors (CCD)."

Consequently, charged coupled detectors are used to assist in analyzing signals from detectors.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the photodetector analyses of Savory et al., Hanai, Chen

et al. and Tomlinson et al. by use of the CCDs of Tacklind et al. because it is obvious to apply a known technique to a known method to yield a predictable result. In this instance, it would have been obvious to apply the known technique of using CCDs to analyze signals to the known method of using photodetectors to measure sample amount as in Savory et al., Hanai, Chen et al. and Tomlinson et al. to yield the predictable result of modified spectra and a modified means of receiving the relevant signals. There would have been a reasonable expectation of success in combining a CCD of Tacklind et al. with the detectors and photodetectors of Savory et al., Hanai, Chen et al. and Tomlinson et al. because the charge coupled device of Tacklind et al. allows an alternative means of measuring the intensities of particles and converting them into electrical signals.

Response to arguments:

Applicant's arguments filed 2 October 2008 have been fully considered and they are persuasive. Applicant argues that the reference of Tacklind et al. does not overcome the alleged deficiencies of Savory et al., Chen et al., and Tomlinson et al. For the reasons discussed above, the newly applied combination of Savory et al., Hanai, Chen et al., and Tomlinson et al. is not deficient and the instant prior art rejection is maintained.

The following rejection is newly applied:

35 U.S.C. 103 Rejection #6:

Claims 27, 39, and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Savory et al. in view of Hanai in view of Chen et al. in view of Tomlinson et al. in view of Tacklind et al. as applied to claims 20, 23-26, 28-29, 33, 34, 36-38, 40-41, 45-49, and 51-52 above, and further in view of Pierre et al. [IEEE Acoustics, Speech, and Signal Processing. 1995, pages 1900-1903].

Claims 27, 39 and 50 are further limiting wherein the scaling of the first output signal comprises multiplying the first output signal value by a ratio of T2/T1.

The studies of Savory et al., Hanai, Chen et al., Tomlinson et al., and Tacklind et al. make obvious the measurement of signals of particle using photodetectors, as discussed above.

The studies of Savory et al., Hanai, Chen et al., Tomlinson et al., and Tacklind et al. do not teach multiplying the signal by a ratio of T2/T1.

The article of Pierre et al. studies the consideration in the autocalibration of quadrature receivers in which Figure 2 on page 1902 of Pierre et al. illustrates a log-log plot of the variance of the signal to noise ratio as a function of the ratio of two times. The purpose of the simulation plotted in Figure 2 of Pierre is to illustrate the variance in signal to noise ratio as observation time increases.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the photodetector analysis of Savory et al., Hanai, Chen et al., Tomlinson et al., and Tacklind et al. by use of the time ratio simulation of Pierre et al. where the motivation would have been that Pierre et al. gives information regarding

signal accuracy (in terms of variance in signal to noise ratio) as a function of observance time [see page 1903 of Pierre et al.]

<u>Response to arguments</u>:

Applicant's arguments filed 2 October 2008 have been fully considered and they are persuasive. Applicant argues that the reference of Pierre et al. does not overcome the alleged deficiencies of Savory et al., Chen et al., Tomlinson et al., and Tacklind et al. For the reasons discussed above, the newly applied combination of Savory et al., Hanai, Chen et al., Tomlinson et al., and Tacklind et al. is not deficient and the instant prior art rejection is maintained.

Double Patenting

<u>The following Double Patenting Rejections are NEWLY applied:</u>

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29

USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Double Patenting Rejection #1:

Claims 33, 34, 36, 37, and 38 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 4, 16, and 18 of U.S. Patent No. 6,894,264. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to using photodetectors to assess biological material (i.e. for sequencing) in order to scale a configuration such that the dynamic range of the photodetector is effectively extended. While claim 1 of '264 recites more detail on how the scaling is accomplished within the claim, claim 1 of '264 still recited the same effecting limitations of scaling recited in

instant claim 33. Additionally, claims 16 and 18 of '264 recite similar claim limitations regarding signals, and specific and different times are recorded and compared (as in instant claims 37 and 38).

Double Patenting Rejection #2:

Claims 36-38 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 4, and 14 of U.S. Patent No. 7,423,251. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to using photodetectors to assess biological material (i.e. for sequencing) in order to scale a configuration such that the dynamic range of the photodetector is effectively extended. Additionally, claim 1 of '251 describes specific and different acquisition times for the signals as recited in instant claims 36-38.

Conclusion

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the central PTO Fax Center. The faxing of such pages must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The Central PTO Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Negin, Ph.D., whose telephone number is (571) 272-1083. The examiner can normally be reached on Monday-Friday from 7am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Marjorie Moran, Supervisory Patent Examiner, can be reached at (571) 272-0720.

Information regarding the status of the application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information on the PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/RSN/
Russell S. Negin
30 October 2008

/Marjorie Moran/
Supervisory Patent Examiner, Art Unit 1631